

**Amendments To The Claims:**

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-111. (cancelled)

Claim 112. (new) A method comprising:

- (a) providing first data from a first set of samples wherein:
  - (i) the first set of samples comprises a plurality of samples classified into a first biological state class and a plurality of samples classified into a second biological state class;
  - (ii) the data from each sample in the first set comprises a plurality of data elements, each data element characterized by a value, wherein all of the samples share a plurality of common data elements;
- (b) performing multivariate analysis on the first data to qualify each common data element in the first data based on the ability of the data element to classify a sample into the first biological state class or the second biological state class, as a function of data element value;
- (c) selecting a first subset of qualified common data elements from the first data;
- (d) providing second data from a second set of samples wherein:
  - (i) the second set of samples comprises a plurality of samples classified into the first biological state class and a plurality of samples classified into the second biological state class;
  - (ii) the data from each sample in the second set comprises a plurality of data elements, each data element characterized by a value, wherein all of the samples share the plurality of common data elements;
  - (iii) the first samples and the second samples come from first and second populations that have a statistically significant difference with respect to at least one preanalytical variable;
- (e) performing multivariate analysis on the second data to qualify each common data element in the second data based on the ability of the data element to classify a sample

into the first biological state class or the second biological state class, as a function of data element value;

- (f) selecting a second subset of qualified common data elements from the second data;
- (g) selecting an intersection subset of data elements from the first and second subsets, wherein each data element in the intersection subset is a member of both of the first and second subsets; and
- (h) displaying the intersection subset on a graphical display interface on a user device.

Claim 113. (new) The method of claim 112 wherein the first and second populations have a statistically significant difference with respect to a preanalytical variable selected from the group consisting of gender, age, ethnicity, sample collection parameter, sample processing parameter, weight, diet, medication status, medical condition, amount of physical exercise, pregnancy, level of circulating antibodies and a clinical characteristic.

Claim 114. (new) The method of claim 113 wherein the first and second populations have a statistically significant difference with respect to a plurality of preanalytical variables selected from said group.

Claims 115. (new) The method of claim 112 wherein the first samples and the second samples are collected from different geographical locations.

Claims 116. (new) The method of claim 112 wherein the first samples and the second samples are collected from different clinical trial sites.

Claim 117. (new) The method of claim 112 wherein the step of selecting the first and second subsets comprises using the discovery data sets to train a learning algorithm wherein the learning algorithm ranks the data elements based on a quantitative measure of ability to classify.

Claim 118. (new) The method of claim 117 wherein the learning algorithm is a supervised learning algorithm.

Claim 119. (new) The method of claim 117 wherein the learning algorithm is an unsupervised learning algorithm.

Claim 120. (new) The method of claim 117 wherein the training comprises using support vector machine analysis.

Claim 121. (new) The method of claim 117 wherein the training comprises performing linear discrimination analysis.

Claim 122. (new) The method of claim 117 wherein the training comprises performing unified maximum separability analysis (UMSA).

Claim 123. (new) The method of claim 112 further comprising independently re-sampling data elements in each data set.

Claim 124. (new) The method of claim 112 further comprising, selecting candidate biomarkers from selected data elements and testing one or more of the candidate biomarkers on a validation data set.

Claim 125. (new) The method of claim 112 wherein the biological state class comprises a cell state.

Claim 126. (new) The method of claim 112 wherein the biological state class is a patient status.

Claim 127. (new) The method of claim 112 wherein the biological state class is selected from the group consisting of: presence of a disease; absence of a disease; progression of a disease; risk for a disease; stage of disease; likelihood of recurrence of disease; a genotype; a

phenotype; exposure to an agent or condition; a demographic characteristic; resistance to agent, sensitivity to an agent, and combinations thereof.

Claim 128. (new) The method of claim 127 wherein the genotype is selected from the group consisting of an HLA haplotype; a mutation in a gene; a modification of a gene, and combinations thereof.

Claim 129. (new) The method of claim 127 wherein the agent is selected from the group consisting of a toxic substance, a potentially toxic substance, an environmental pollutant, a candidate drug, and a known drug.

Claim 130. (new) The method of claim 127 wherein sensitivity to an agent comprises responsiveness to a drug.

Claim 131. (new) The method of claim 124 wherein the one or more candidate biomarkers are diagnostic of the presence of a disease, risk of developing a disease, risk of recurrence of a disease, or stage of the disease.

Claim 132. (new) The method of claim 112 wherein values of the data elements in a data point represent levels and/or frequency of components in a data point sample.

Claim 133. (new) The method of claim 132 wherein components are selected from the group consisting of: nucleic acids, proteins, polypeptides, peptides, carbohydrates and modified or processed forms thereof.

Claim 134. (new) The method of claim 112 wherein levels of components are measured by an expression profiling assay.

Claim 135. (new) The method of claim 134 wherein the expression profiling assay comprises measuring the amount and/or form of a nucleic acid.

Claim 136. (new) The method of claim 134 wherein expression profiling comprises measuring amplification, mutation, and/or modification of DNA.

Claim 137. (new) The method of claim 134 wherein the expression profiling assay comprises measuring the amount and/or form of a protein, polypeptide or peptide.

Claim 138. (new) The method of claim 137 wherein the expression profiling assay comprises mass spectrometry.

Claim 139. (new) The method of claim 138 wherein the expression profiling assay comprises SELDI analysis.

Claim 140. (new) The method of claim 134 wherein the expression profiling assay comprises measuring the amount and/or form of a carbohydrate.

Claim 141. (new) The method of claim 112 wherein expression profiling comprises:

- (a) contacting samples with a substrate comprising binding partners for specifically binding to sample components having selected characteristics and
- (b) identifying sample components bound to the substrate.

Claim 142. (new) The method of claim 141 wherein binding partners are selected from the group consisting of cationic molecules; anionic molecules; metal chelates; antibodies; single- or double-stranded nucleic acids; proteins, peptides, amino acids; carbohydrates; lipopolysaccharides; sugar amino acid hybrids; molecules from phage display libraries; biotin; avidin; streptavidin; and combinations thereof.

Claim 143. (new) The method of claim 141 wherein the binding partners are arrayed on the substrate.

Claim 144. (new) The method of claim 117 wherein an assay used to measure levels of data elements in training data sets from which candidate biomarkers are identified is different from an assay used to measure data elements in a validation data set used to validate the candidate biomarker.

Claim 145. (new) The method of claim 140 wherein the assay used to measure levels of data elements in training data sets is SELDI.

Claim 146. (new) The method of claim 140 wherein the assay used to measure levels of data elements in validation data sets is an immunoassay.

Claim 147. (new) The method of claim 112 wherein the independent discovery data sets are collected from different locations, using different collection protocols, and/or are collected from different populations.

Claim 148. (new) The method of claim 112 wherein each discovery data set is from a different clinical trial site.

Claim 149. (new) A computer program product comprising a computer readable medium having:

- (a) receiving input data relating to at least first and second independent discovery data sets wherein:
  - (i) the data sets comprise a plurality of forms of biological state classes;
  - (ii) each data set comprises a plurality of data points, wherein each data point exhibits one form of a biological state class and each data set comprises a plurality of data points belonging to each of the classes; and
  - (iii) each data point comprises a plurality of data elements, each data element characterized by a value, wherein all data points share a plurality of common data elements;

(b) a second computer readable program code providing instructions for qualifying each common data element, independently for each data set, based on the ability of the data element to classify a data point into a biological state class, as a function of data element value and for selecting an initial subset of data elements within each data set, and

(c) a third computer readable program code providing instructions for selecting an intersection subset of data elements from the initial subsets, wherein each data element in the intersection subset is a member of a majority of the initial subsets.

Claim 150. (new) The computer program product of claim 149 wherein selecting the initial subsets comprises using the discovery data sets to train a learning algorithm wherein the learning algorithm ranks the data elements based on a quantitative measure of ability to classify.

Claim 151. (new) The computer program product of claim 149 wherein the learning algorithm is a supervised learning algorithm.

Claim 152. (new) The computer program product of claim 149 wherein the learning algorithm is an unsupervised learning algorithm.

Claim 153. (new) The computer program product of claim 150 wherein training comprises support vector machine analysis.

Claim 154. (new) The computer program product of claim 150 wherein training comprises linear discrimination analysis.

Claim 155. (new) The computer program product of claim 150 wherein training comprises combining support vector machine analysis and linear discrimination analysis.

Claim 156. (new) The computer program product of claim 150 wherein training comprises performing unified maximum separability analysis (UMSA).

Claim 157. (new) The computer program product of claim 149 further comprising program code for independently re-sampling data elements in each data set.

Claim 158. (new) The computer program product of claim 149 further comprising program code for selecting candidate biomarkers based on ranking by the learning algorithm and for testing one or more of the candidate biomarkers on a validation data set.

Claim 159. (new) The computer program product of claim 149 wherein the biological state class comprises a cell state.

Claim 160. (new) The computer program product of claim 149 wherein the biological state class comprises a patient status.

Claim 161. (new) The computer program product of claim 149 wherein the biological state class is selected from the group consisting of: presence of a disease; absence of a disease; progression of a disease; risk for a disease; stage of disease; likelihood of recurrence of disease; a genotype; a phenotype; exposure to an agent or condition; a demographic characteristic; resistance to agent, sensitivity to an agent, and combinations thereof.

Claim 162. (new) The computer program product of claim 161 wherein the genotype is selected from the group consisting of an HLA haplotype; a mutation in a gene; a modification of a gene, and combinations thereof.

Claim 163. (new) The computer program product of claim 161 wherein the agent is selected from the group consisting of a toxic substance, a potentially toxic substance, an environmental pollutant, a candidate drug, and a known drug.

Claim 164. (new) The computer program product of claim 161 wherein sensitivity to an agent comprises responsiveness to a drug.



Claim 165. (new) The computer program product of claim 158 wherein the one or more candidate biomarkers are diagnostic of the presence of a disease, risk of developing a disease, risk of recurrence of a disease, or stage of the disease.

Claim 166. (new) The computer program product of claim 161 wherein values of the data elements in a data point represent levels and/or frequency of components in a data point sample.

Claim 167. (new) The computer program product of claim 161 wherein components are selected from the group consisting of: nucleic acids, proteins, polypeptides, peptides, carbohydrates and modified or processed forms thereof.

Claim 168. (new) The computer program product of claim 160 wherein levels of components are measured by an expression profiling assay.

Claim 169. (new) The computer program product of claim 168 wherein the expression profiling assay comprises measuring the amount and/or form of a nucleic acid.

Claim 170. (new) The computer program product of claim 168 wherein expression profiling comprises measuring amplification, mutation, and/or modification of DNA.

Claim 171. (new) The computer program product of claim 168 wherein the expression profiling assay comprises measuring the amount and/or form of a protein, polypeptide or peptide.

Claim 172. (new) The computer program product of claim 168 wherein the expression profiling assay comprises mass spectrometry.

Claim 173. (new) The computer program product of claim 168 wherein the expression profiling assay comprises SELDI analysis.

Claim 174. (new) The computer program product of claim 168 wherein the expression profiling assay comprises measuring the amount and/or form of a carbohydrate.

Claim 175. (new) The computer program product of claim 168 wherein expression profiling comprises:

- (a) contacting samples with a substrate comprising binding partners for specifically binding to sample components having selected characteristics; and
- (b) identifying sample components bound to the substrate.

Claim 176. (new) The computer program product of claim 175 wherein binding partners are selected from the group consisting of cationic molecules; anionic molecules; metal chelates; antibodies; single- or double-stranded nucleic acids; proteins, peptides, amino acids; carbohydrates; lipopolysaccharides; sugar amino acid hybrids; molecules from phage display libraries; biotin; avidin; streptavidin; and combinations thereof.

Claim 177. (new) The computer program product of claim 149 wherein an assay used to measure levels of data elements in training data sets from which candidate biomarkers are identified is different from an assay used to measure data elements in a validation data set used to validate the candidate biomarker.

Claim 178. (new) The computer program product of claim 149 wherein the assay used to measure levels of data elements in training data sets is SELDI.

Claim 179. (new) The computer program product of claim 149 wherein the assay used to measure levels of data elements in validation data sets is an immunoassay.

Claim 180. (new) The computer program product of claim 149 wherein the independent discovery data sets are collected from different locations, using different collection protocols, and/or are collected from different populations.

Claim 181. (new) The computer program product of claim 149 wherein each discovery data set is from a different clinical trial site.

Claim 182. (new) A system comprising:

one or more processors for

(a) receiving input data relating to at least first and second independent discovery data sets wherein:

(i) the first set of samples comprises a plurality of samples classified into a first biological state class and a plurality of samples classified into a second biological state class;

(ii) the data from each sample in the first set comprises a plurality of data elements, each data element characterized by a value, wherein all of the samples share a plurality of common data elements;

(iii) the second set of samples comprises a plurality of samples classified into the first biological state class and a plurality of samples classified into the second biological state class;

(iv) the data from each sample in the second set comprises a plurality of data elements, each data element characterized by a value, wherein all of the samples share the plurality of common data elements;

(b) executing computer readable program code providing instructions for qualifying each common data element, independently for each data set, based on the ability of the data element to classify a data point into a biological state class, as a function of data element value and for selecting an initial subset of data elements within each data set; and

(c) executing computer readable program code providing instructions for selecting an intersection subset of data elements from the initial subsets, wherein each data element in the intersection subset is a member of a majority of the initial subsets.

Claim 183. (new) The system of claim 182 further comprising one or more devices for providing input data to the one or more processors.

Claim 184. (new) The system of claim 182 wherein the one or more devices for providing input data comprises a detector for detecting a characteristic of a data element.

Claim 185. (new) The system of claim 182 wherein the detector comprises a mass spectrometer.

Claim 186. (new) The system of claim 182 wherein the detector comprises a gene chip reader.

Claim 187. (new) The system of claim 182 further comprising a memory for storing a data set of ranked data elements.

Claim 188. (new) The system of claim 182 further comprising a database of ranked data elements.

Claim 189. (new) The system of claim 182 wherein selecting the initial subsets comprises using the discovery data sets to train a learning algorithm wherein the learning algorithm ranks the data elements based on a quantitative measure of ability to classify.

Claim 190. (new) The system of claim 189 wherein the learning algorithm is a supervised learning algorithm.

Claim 191. (new) The system of claim 189 wherein the learning algorithm is an unsupervised learning algorithm.

Claim 192. (new) The system of claim 189 wherein training comprises support vector machine analysis.

Claim 193. (new) The system of claim 189 wherein training comprises linear discrimination analysis.

Claim 194. (new) The system of claim 189 wherein training comprises combining support vector machine analysis and linear discrimination analysis.

Claim 195. (new) The system of claim 189 wherein training comprises performing unified maximum separability analysis (UMSA).

Claim 196. (new) The system of claim 182 wherein the system further executes program code for independently re-sampling data elements in each data set.

Claim 197. (new) The system of claim 189 wherein the system further executes program code for selecting candidate biomarkers based on ranking by the learning algorithm and for testing one or more of the candidate biomarkers on a validation data set.

Claim 198. (new) The system of claim 182 wherein the biological state class comprises a cell state.

Claim 199. (new) The system of claim 182 wherein the biological state class comprises a patient status.

Claim 200. (new) The system of claim 182 wherein the biological state class is selected from the group consisting of: presence of a disease; absence of a disease; progression of a disease; risk for a disease; stage of disease; likelihood of recurrence of disease; a genotype; a phenotype; exposure to an agent or condition; a demographic characteristic; resistance to agent, sensitivity to an agent, and combinations thereof.

Claim 201. (new) The system of claim 200 wherein the genotype is selected from the group consisting of an HLA haplotype; a mutation in a gene; a modification of a gene, and combinations thereof.

Claim 202. (new) The system of claim 200 wherein the agent is selected from the group consisting of a toxic substance, a potentially toxic substance, an environmental pollutant, a candidate drug, and a known drug.

Claim 203. (new) The system of claim 200 wherein sensitivity to an agent comprises responsiveness to a drug.

Claim 204. (new) The system of claim 197 wherein the one or more candidate biomarkers are diagnostic of the presence of a disease, risk of developing a disease, risk of recurrence of a disease, or stage of the disease.

Claim 205. (new) The system of claim 182 wherein values of the data elements in a data point represent levels and/or frequency of components in a data point sample.

Claim 206. (new) The system of claim 205 wherein components are selected from the group consisting of: nucleic acids, proteins, polypeptides, peptides, carbohydrates and modified or processed forms thereof.

Claim 207. (new) The system of claim 205 wherein levels of components are measured by an expression profiling assay.

Claim 208. (new) The system of claim 207 wherein the expression profiling assay comprises measuring the amount and/or form of a nucleic acid.

Claim 209. (new) The system of claim 207 wherein expression profiling comprises measuring amplification, mutation, and/or modification of DNA.

Claim 210. (new) The system of claim 207 wherein the expression profiling assay comprises measuring the amount and/or form of a protein, polypeptide or peptide.

Claim 211. (new) The system of claim 207 wherein the expression profiling assay comprises mass spectrometry.

Claim 212. (new) The system of claim 214 wherein the expression profiling assay comprises SELDI analysis.

Claim 213. (new) The system of claim 207 wherein the expression profiling assay comprises measuring the amount and/or form of a carbohydrate.

Claim 214. (new) The system of claim 207 wherein expression profiling comprises:

- (a) contacting samples with a substrate comprising binding partners for specifically binding to sample components having selected characteristics and
- (b) identifying sample components bound to the substrate.

Claim 215. (new) The system of claim 214 wherein binding partners are selected from the group consisting of cationic molecules; anionic molecules; metal chelates; antibodies; single- or double-stranded nucleic acids; proteins, peptides, amino acids; carbohydrates; lipopolysaccharides; sugar amino acid hybrids; molecules from phage display libraries; biotin; avidin; streptavidin; and combinations thereof.

Claim 216. (new) The system of claim 182 wherein an assay used to measure levels of data elements in training data sets from which candidate biomarkers are identified is different from an assay used to measure data elements in a validation data set used to validate the candidate biomarker.

Claim 217. (new) The system of claim 216 wherein the assay used to measure levels of data elements in training data sets is SELDI.

Claim 218. (new) The system of claim 216 wherein the assay used to measure levels of data elements in validation data sets is an immunoassay.

Claim 219. (new) The system of claim 182 wherein the independent discovery data sets are collected from different locations, using different collection protocols, and/or are collected from different populations.

Claim 220. (new) The system of claim 182 wherein each discovery data set is from a different clinical trial site.